REMARKS

This application is a 371 filing of PCT International application no. PCT/EP2003/012129 filed October 31, 2003. Original claims 1-12 of the priority application were cancelled by Preliminary Amendment at the time of filing and new claim 13 was added. In response to an initial Office Action, claim 13 was amended above and new claims 14-17 were added. Claims 13-17 remain pending in the application.

Rejection under 35 U.S.C. §102

Claims 13-17 are rejected under 35 U.S.C. §102(b) as being anticipated by Parmentier et al. According to the Office Action, Parmentier et al. teach that the antibody used in the method to detect TSH receptor is purified polyclonal autoantibody against TSH receptor from serum of patients with Graves' Disease (GD). The Office Action maintains that Applicants' recitation of "affinity purified polyclonal human autoantibodies" amounts to a product-by-process limitation that does not distinguish over Parmentier et al., and that Parmentier et al., therefore anticipates the claims of the present application. Applicants respectfully disagree.

Parmentier et al. is the first disclosure of the complete DNA and amino acid sequences of the TSH receptor. Additionally, Parmentier et al. contains several proposals how the new sequence information could be exploited, including the preparation of antibodies and assays using the antibodies. According to Parmentier et al. because of the particular antigenic nature of the TSHr polypeptide, it is useful in preparing anti-TSHr antibodies in an animal, for example, by immunizing a rabbit or mouse with the polypeptide. In Applicants' view, specific reference by Parmentier et al. to these species, the classic models for immunization-induced antibody production, suggests that Parmentier et al. was referring to experimentally induced antibodies ***not*** naturally occurring ***auto***antibodies isolated from GD patient sera. Furthermore, with respect to the use of TSHr in an assay for the quantitative detection of TSH or anti-TSHr antibodies, Parmentier et al. contains no mention of ***auto***antibodies. Overall, it does not appear that Parmentier et al. contemplated the use of naturally occurring ***auto***antibodies that are isolated from GD patient sera for use in immunoassays.

In support of this conclusion, Applicants point to the disclosure at column 14, line 52 to column 15, line, the only teaching in Parmentier et al. that specifically mentions use of autoantibodies (immunoglobulins) from Graves' disease patients. Firstly, the assay in Parmentier et al. is based on the competition between the receptor's natural ligand, TSH, and thyroid stimulating immunoglobulins prepared from patient sera; the assay uses labeled TSH ([^{125}I] TSH) as the reporter molecule.

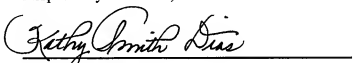
Conversely, in Applicants' claimed method, the assay uses affinity purified GD patient-derived autoantibodies that are labeled; thus, the assay is based on the competition between affinity purified GD patient-derived autoantibodies and anti-TSHr autoantibodies in a biological sample to be assayed. Parmentier does not teach this feature of Applicants' claimed method.

Secondly, Parmentier observed that one of two autoantibody preparations from GD patients examined (only two were tested) exhibited limited ability to displace labeled TSH under the conditions of the assay (GD2 in Figure 10). Based on this teaching, Applicants think it unlikely that one of skill in the art would conclude that the use of GD patient-derived autoantibodies would be a desirable competitor/reporter in an assay system to detect anti-TSHr autoantibodies as claimed by the present invention.

Parmentier et al. neither teaches nor suggests a method for detection of anti-TSHr autoantibodies using anti-TSHr ***auto***antibodies as the competitive detection agent; that is, Parmentier et al. does not teach contacting a biological sample with TSH receptor in the presence of labeled affinity-purified polyclonal human ***auto***antibodies against the receptor as recited in step a of independent claim 1. Parmentier et al. does not contemplate the use of anti-TSHr ***auto***antibodies in an immunoassay and, therefore, cannot anticipate the claimed invention. Accordingly, withdrawal of the rejection under 35 U.S.C. §102 is respectfully requested.

It is respectfully submitted that the above-identified application is now in condition for allowance and favorable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, she is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,



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